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REVIEW ARTICLE ON HUMAN MONKEYPOX VIRUS

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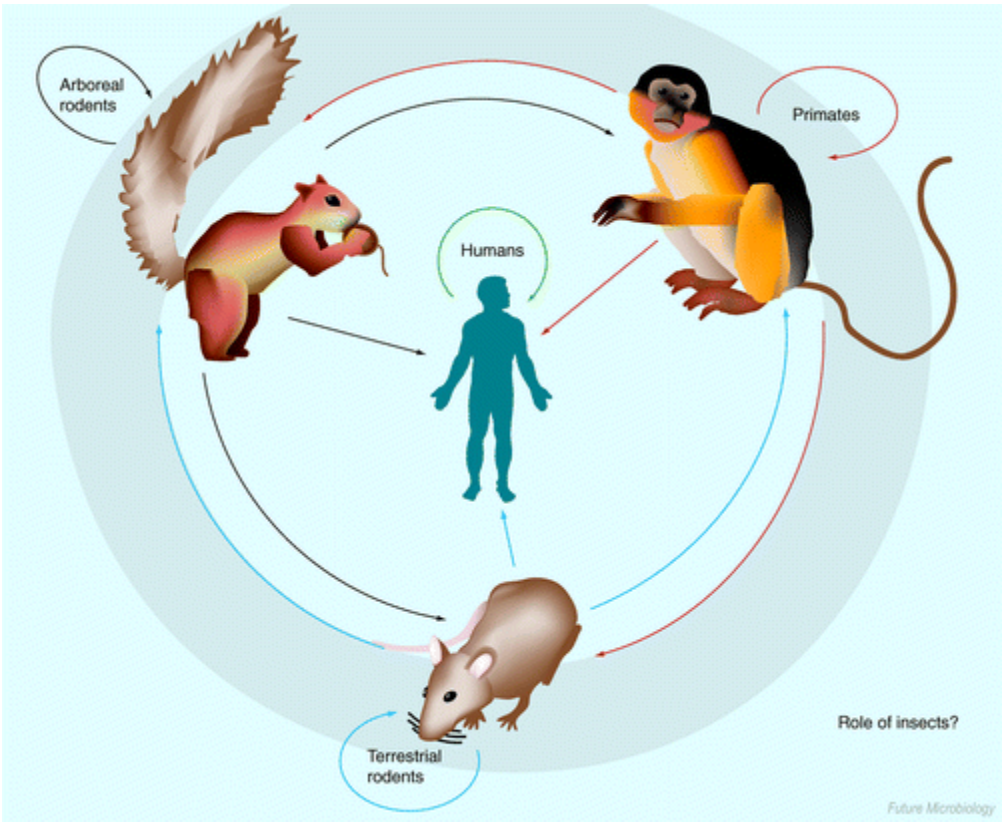
ABSTRACT

Human monkeypox is a rare viral zoonosis endemic to central and western Africa that has recently emerged in the USA. Laboratory diagnosis is important because the virus can cause disease that is clinically indistinguishable from other pox-like illnesses, particularly smallpox and chickenpox. Although the natural animal reservoir of the monkeypox virus is unknown, rodents are the probable source of its introduction into the USA. A clear understanding of the virulence and transmissibility of human monkeypox has been limited by inconsistencies in epidemiological investigations. Monkeypox is the most important orthopoxvirus infection in human beings since the eradication of smallpox in the 1970s. There is currently no proven treatment for human monkeypox, and questions about its potential as an agent of bioterrorism persist. New therapeutics and vaccines offer hope for the treatment and prevention of monkeypox; however, more research mus be done before they are ready to be developed in an endemic setting. There is a need for more research in the epidemiology, ecology, and biology of the virus in endemic areas to better understand and prevent human infections.

INTRODUCTION

Monkeypox is an infectious illness caused by the monkeypox virus. It is a viral zoonotic infection that is it can spread from infected animals to humans. It can also spread from infected person to person. Monkeypox is an orthopox virus genus and is closely related to smallpox, endemic to parts of Africa. Despite the name, the natural hosts appear to be rodents. Genetic analysis suggests that there are two distinct lineages of monkeypox (with different virulence for humans). In the United States in 2003 an outbreak of monkeypox was associated with pet prairie dogs. By the end of the outbreak, the CDC (Center for Disease

Control and Prevention) reported 47 cases (37 confirmed and an additional 10 probable human cases). The cases were relatively mild (no deaths) but the outbreak prompted a significant response and investigation. How did monkeypox, an African virus, come to find its way into prairie dogs in the United States? The introduction on monkeypox was traced to importation of a large shipment of wild caught small mammals (including rodents), from West Africa. Some of those rodents found their way to a prairie dog breeder and all infected persons had purchased pet prairie dogs. This incident serves as an example of the danger of importing exotic wild animals for the pet trade.



History

Since it was first identified in a colony of monkeys in Copenhagen, Denmark in 1958, monkeypox has been largely overlooked by the Western world.

Monkeypox virus was first observed in humans from West and Central Africa in the 1970s at the time that smallpox had been eradicated from the area. Monkeypox was first recognized by Von Magnus. The disease was later seen in other captive animals including primates in zoos and animal import centers. Particular attention was focused on it in 1970 when smallpox surveillance activities in Africa revealed cases of human monkeypox,

clinically indistinguishable from smallpox, particularly in Zaire (now the Democratic Republic of the Congo [DRC]). Serosurveys and virologic investigations in the 1980s in the DRC by the WHO indicated that monkeys are sporadically infected, as are humans; three-fourths of cases, mainly in children younger than 15 years, resulted from animal contact.

Human monkeypox has continued to be reported from the DRC, mainly in children younger than 15 years. On the basis of reported monkeypox onset dates in a largely retrospective study complicated by a concurrent outbreak of chickenpox, about 250 serosubstantiated cases of monkeypox occurred among 0.5 million people in 78 villages, from February 1996 to October 1997. About three-fourths of the cases appeared to result from human-to-human transmission;

Human monkeypox cases were first detected in 1970 in a 9 month old boy in a region where smallpox had been eliminated in 1968 and studied intensively by WHO teams throughout the 1980s. They documented the fact that the natural monkeypox virus reservoir was actually ground squirrels and that man only infrequently became infected. However, the teams discovered that the virus could be passed from person to person although it was much less contagious than was smallpox. Moreover, the studies indicated that it was highly unlikely that the virus could continue to spread even in populations that had never been vaccinated.

During 1997–98, reports of large outbreaks of human monkeypox cases in the Democratic Republic of the Congo raised questions as to whether monkeypox might be spreading so readily from person to person as to replace smallpox as a dangerous contagious disease. The reports in 1997 of large numbers of human monkeypox cases were widely publicized and caused alarm. However, as investigations progressed, it became clear that a large proportion of the cases were chickenpox and that there was little evidence to suggest that the virus had changed its character. However, field studies could not be pursued because of civil strife until very recently. As of 2007, intensive surveillance for cases throughout a large area in the Democratic Republic of the Congo have been resumed but evidence of more frequent human-to-human spread has not been detected.

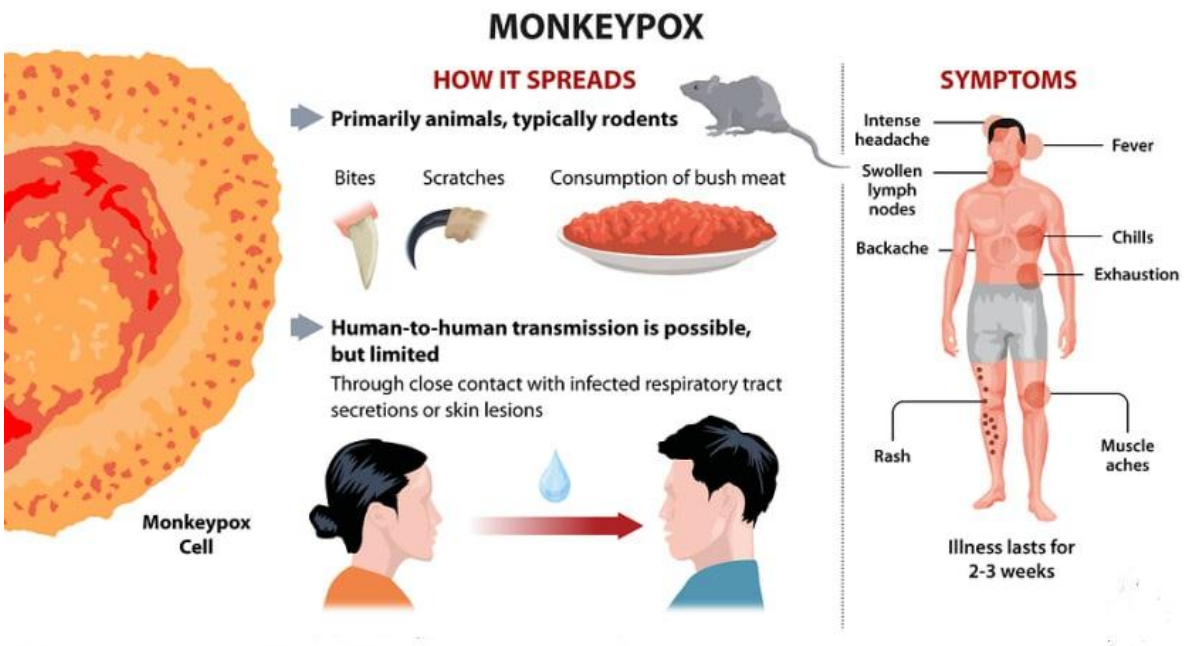
India’s first monkeypox case has been reported from Kerala in 35year old male. The patient travelled from UAE and reached to the Kerala.

Etiology

Since the eradication of smallpox (variola), monkey pox virus, causing the disease monkey pox, has, for humans, become the most important member of the genus *Orthopoxvirus*. Monkeys are the predominant host for the virus; however, it may be endemic in African rainforest squirrels and is present in African rats, mice, domestic pigs, hedgehogs, and opossums. It has also been identified in and transmitted by prairie dogs in the United States and has affected elephants in zoos. Severity of infection varies by viral strain and by host; for example, disease is relatively mild in cynomolgus monkeys but severe in orangutans. Monkeypox is spread when you come into contact with an animal or a person infected with the virus. Animal-to-person transmission occurs through broken skin, like from bites or scratches or through direct contact with an infected animal's blood, bodily fluids or pox lesions (sores).

Monkeypox can spread from person to person, but it's less common. Person-to-person spread (transmission) occurs when you come in contact with the sores, scabs, respiratory droplets or oral fluids of an infected person usually through close, intimate situations like cuddling, kissing or sex. Research is ongoing, but researchers aren't sure if the virus is transmitted through semen or vaginal fluids.

You can also get monkey pox by coming into contact with recently contaminated materials like clothing, bedding and other linens used by an infected person or animal.



Monkeypox is a rare disease caused by infection with the monkeypox virus. Monkeypox virus is part of the same family of viruses as smallpox. Monkeypox symptoms are similar to smallpox symptoms, but milder; and monkeypox is rarely fatal. Monkeypox is not related to chickenpox.

❖ **Symptoms of monkeypox include**

- High temperature
- Headache
- Muscle aches and backache
- Dry cough
- Sour throat
- Swollen lymph nodes
- Chills/shivering
- Exhaustion
- As per some experts, lesions associated with monkeypox can be seen in the respiratory tract before being spotted on other body parts.
- A rash that can look like pimples or blisters field with fluid that appears on the face, inside the mouth, and on other parts of the body, like the hands, feet, chest, genitals, or anus.

The rash goes through different stages before healing completely. The illness typically lasts 2-4 weeks. Sometimes, people get a rash first, followed by other symptoms. Others only experience a rash.

Treatment

Currently there is no treatment approved specifically for monkeypox virus infections. However, antivirals developed for use in patients with smallpox may prove beneficial against monkeypox. The following medical countermeasures are currently available from the Strategic National Stockpile (SNS) as options for the treatment of monkeypox:

Tecovirimat (also known as TPOXX, ST-246)

TPOXX is an antiviral medication that is approved by the United States Food and Drug Administration (FDA) [PDF – 24 pages] for the treatment of smallpox in adults and children. Data are not available on the effectiveness of tecovirimat in treating monkeypox infections in people, but studies using a variety of animal species have shown that tecovirimat is effective

in treating disease caused by orthopoxviruses. Clinical trials in people showed the drug was safe and had only minor side effects. CDC holds an expanded access protocol (sometimes called "compassionate use") that allows for the use of stockpiled Tecovirimat to treat monkeypox during an outbreak. Tecovirimat is available as a pill or an injection. For children who weigh less than 28.6 pounds, the capsule can be opened, and medicine mixed with semi-solid food.

Cidofovir (also known as Vistide)

Cidofovir is an antiviral medication that is approved by the FDA\for the treatment of cytomegalovirus (CMV) retinitis in patients with Acquired Immunodeficiency Syndrome (AIDS). Data is not available on the effectiveness of Cidofovir in treating human cases of monkeypox. However, it has shown to be effective against orthopoxviruses in *in vitro* and animal studies. CDC holds an expanded access protocol that allows for the use of stockpiled Cidofovir for the treatment of orthopoxviruses (including monkeypox) in an outbreak. It is unknown whether or not a person with severe monkeypox infection will benefit from treatment with Cidofovir, although its use may be considered in such instances. Brincidofovir may have an improved safety profile over Cidofovir. Serious renal toxicity or other adverse events have not been observed during treatment of cytomegalovirus infections with Brincidofovir as compared to treatment using Cidofovir.

Brincidofovir (also known as CMX001 or Tembexa)

Brincidofovir is an antiviral medication that was approved by the FDA [PDF – 21 pages] on June 4, 2021 for the treatment of human smallpox disease in adult and pediatric patients, including neonates. Data is not available on the effectiveness of Brincidofovir in treating cases of monkeypox in people. However, it has shown to be effective against orthopoxviruses in *in vitro* and animal studies. CDC is currently developing an EA-IND to help facilitate use of Brincidofovir as a treatment for monkeypox. However, Brincidofovir is not currently available from the SNS.

State and territorial health authorities can direct their requests for medical countermeasures for the treatment of monkeypox to the CDC Emergency Operations Center.

Prevention

- **Vaccination**

Vaccination against smallpox is assumed to provide protection against human monkeypox infection because they are closely related viruses and the vaccine protects animals from experimental lethal monkeypox challenges. This has not been conclusively demonstrated in humans because routine smallpox vaccination was discontinued following the eradication of smallpox.

Smallpox vaccine has been reported to reduce the risk of monkeypox among previously vaccinated persons in Africa. The decrease in immunity to poxviruses in exposed populations is a factor in the prevalence of monkeypox. It is attributed both to waning cross-protective immunity among those vaccinated before 1980 when mass smallpox vaccinations were discontinued, and to the gradually increasing proportion of unvaccinated individuals.

The United States Centers for Disease Control and Prevention (CDC) recommends that persons investigating monkeypox outbreaks and involved in caring for infected individuals or animals should receive a smallpox vaccination to protect against monkeypox. Persons who have had close or intimate contact with individuals or animals confirmed to have monkeypox should also be vaccinated.

The smallpox vaccine is said to be 85% effective in treating the illness. US is distributing the Jynneos vaccine, which is a smallpox and monkeypox vaccine (Live, Nonreplicating). The vaccine is administered in two doses and delivered 28 days apart. Just like the precautions we followed during a COVID infection, experts suggest social distancing, masking, improved ventilation and staying at home if sick are some of the recommended methods to follow. Everytime such viruses rear their ugly heads, we are reminded that humans and animals are connected in a complex manner, one in which 2/3rd of the emerging infectious diseases in human beings are zoonotic (trasmitted from animals to humans).

Vaccinia Immune Globulin Intravenous (VIGIV)

VIGIV is licensed by FDA for the treatment of complications due to vaccinia vaccination including eczema vaccinatum, progressive vaccinia, severe generalized vaccinia, vaccinia infections in individuals who have skin conditions, and aberrant infections induced by vaccinia virus (except in cases of isolated keratitis). CDC holds an expanded access protocol

that allows the use of VIGIV for the treatment of orthopoxviruses (including monkeypox) in an outbreak.

Data are not available on the effectiveness of VIG in treatment of monkeypox virus infection. Use of VIG has no proven benefit in the treatment of monkeypox and it is unknown whether a person with severe monkeypox infection will benefit from treatment with VIG. However, healthcare providers may consider its use in severe cases.

VIG can be considered for prophylactic use in an exposed person with severe immunodeficiency in T-cell function for which smallpox vaccination following exposure to monkeypox virus is contraindicated.

- **Avoid contact with people who have suspected or confirmed monkeypox;** Avoid physical contact with anyone who have suspected or confirmed monkeypox; Avoid crowded events; Follow good hygiene; Wear mask.
- **Wash your hands often with soap and water or use an alcohol-based hand sanitizer**. In Central and West Africa, avoid contact with animals that can spread monkeypox virus, usually rodents and primates. Also, avoid sick or dead animals, as well as bedding or other materials they have touched.
- **Raising awareness** of risk factors and educating people about the measures they can take to reduce exposure to the virus is the main prevention strategy for monkeypox. Scientific studies are now underway to assess the feasibility and appropriateness of vaccination for the prevention and control of monkeypox. Some countries have, or are developing, policies to offer vaccine to persons who may be at risk such as laboratory personnel, rapid response teams and health workers.
- **Preventing monkeypox through restrictions on animal trade**

Some countries have put in place regulations restricting importation of rodents and non-human primates. Captive animals that are potentially infected with monkeypox should be isolated from other animals and placed into immediate quarantine. Any animals that might have come into contact with an infected animal should be quarantined, handled with standard precautions and observed for monkeypox symptoms for 30 days.

❖ **Similarities between monkeypox and smallpox**

The clinical presentation of monkeypox resembles that of smallpox, a related orthopoxvirus infection which has been eradicated. Smallpox was more easily transmitted and more often

fatal as about 30% of patients died. The last case of naturally acquired smallpox occurred in 1977, and in 1980 smallpox was declared to have been eradicated worldwide after a global campaign of vaccination and containment. It has been 40 or more years since all countries ceased routine smallpox vaccination with vaccinia-based vaccines. As vaccination also protected against monkey pox in west and central Africa, unvaccinated populations are now also more susceptible to monkey pox virus infection.

Whereas smallpox no longer occurs naturally, the global health sector remains vigilant in the event it could reappear through natural mechanisms, laboratory accident or deliberate release. To ensure global preparedness in the event of reemergence of smallpox, newer vaccines, diagnostics and antiviral agents are being developed. These may also now prove useful for prevention and control of monkeypox.

CONCLUSION

Human monkeypox has the potential for spread via zoonotic reservoirs, as was demonstrated by the US outbreak. Civil conflict and displacements cause concerns for movement of the virus into an area without monkeypox or movement of individuals to more heavily forested areas more prone for interaction with wildlife and a range of zoonoses. The documented rise in incidence of human disease needs further evaluation and consideration with additional studies to better understand the range of factors involved in disease transmission and spread. There are still many unanswered questions about human disease, animal reservoirs, and the virus itself—advances in our understanding of this important zoonosis will help better guide prevention strategies and mitigate human disease.

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